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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/533,895	09/26/1995	SUZANNE L. TOPALIAN	2026-4205	1007

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EXAMINER	
DECLOUX, AMY M	
ART UNIT	**PAPER NUMBER**
1644	40

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	08/533,895	TOPALIAN ET AL.	
	Examin r	Art Unit	
	Amy M. DeCloux	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *100-137* is/are pending in the application.

4a) Of the above claim(s) *118-126 and 128-136* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *100-106,112-117,127 and 137* is/are rejected.

7)☒ Claim(s) *107-111* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 1995* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Notice to Comply with Requirements for Sequence Disclosures

DETAILED ACTION

Applicant's amendment filed 11-22-02, Paper No. 38, is acknowledged and has been entered.

Applicant cancelled all pending claims and added new claims 100-137, claims 118-137 comprising method claims. It is noted that the method claims pending as of the last office action were drawn to a method of preventing or treating melanoma comprising administering one of the claimed peptide compositions. Newly added method claims 118-137 are all drawn to a method of inducing CD4+ T lymphocytes to respond to melanoma cells. Because the cancelled and newly added method claims have distinct endpoints, they are patentably distinct. Because the newly added method claims are patentably distinct from the now cancelled method claims, the newly added method claims are drawn to an invention that was non-elected by original presentation.

Therefore, claims 118-126 and 128-136 are withdrawn from consideration as being drawn to a non-elected invention. Newly added method claims 127 and 137 are not withdrawn and will be considered in the instant office action because the method steps are identical to method steps examined in the previous office action.

In view of Applicant's amendment, all outstanding rejections have been withdrawn and a new grounds of rejection applied, necessitated by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 100-106, 112-117, 127 and 137 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims encompass an immunogenic peptide consisting essentially of amino acids 56-70 of SEQ ID NO:39 or amino acids 448-462 of SEQ ID NO:39 or a derivative thereof that is at least 85% identical with the immunogenic peptide, wherein the immunogenic peptide or derivative thereof is recognized by a CD4+ T lymphocyte which is restricted by a MHC Class II molecule, and a method of administering a composition comprising said peptide or derivative, wherein said peptide consists essentially of a sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:6 (claims 100, 112-117, 127 and 137), SEQ ID NO:4 (claim

101), SEQ ID NO:3 (claim 102), SEQ ID NO:10 (claim 103), SEQ ID NO:11 (claim 104), SEQ ID NO:12 (claim 105), and SEQ ID NOs: 8, 9, 18 and 19 (claim 106).

MPEP 2111.03 states that for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103,absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963).

Since the phrase "consisting essentially of" is being interpreted as comprises, the recited peptide and derivative thereof, can also encompass an indeterminate number and type of additional amino acids, in addition to the amino acids set forth in the recited SEQ ID NO:s 1 and 6. Furthermore, the recitation of peptide derivatives wherein the derivative is at least 85 % identical with the immunogenic peptide encompasses peptides with an indeterminate number and type of additional amino acids, and can conceivably lack the anchor residues necessary to bind MHC Class II molecules.

With the exception of peptides consisting of SEQ ID NO:s 1-4, 6, 8-13, 18-19, there is no description of the required structural and specific immunogenic functional features of the wide range of peptides encompassed by the instant claims, or of the conserved regions that would be critical for these features. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the peptides encompassed. Therefore, the structure of an MHC class II immunogenic peptide, wherein said peptide consists essentially of amino acids 56-70 of SEQ ID NO:39 or amino acids 448-462 of SEQ ID NO:39 or a derivative thereof, is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus an MHC class II immunogenic peptide, or derivative thereof, without further description from the instant specification.

Claims 114-115, 117 and 137 encompass the above peptides linked to an MHC Class II molecule. However, the instant specification only describes the human MHC Class II molecule of HLA-DR-BR 0401 as the presenting molecule for the recited peptides consisting of SEQ ID NO:s 1-5 (Figure 5 and page 12). The prior art does not teach that said peptides can be presented by any other MHC Class II molecule. Though Rammensee teaches that there is some degeneracy in the binding of peptides to MHC Class II, it would not be readily apparent which, if any, of the recited genus of MHC Class II binding peptides could bind an MHC Class II molecule other than HLA-DR-BR 0401, without further description from the specification. Therefore, one of skill would not recognize from the disclosure that applicant was in possession of the genus molecules comprising the recited peptides and an MHC class II molecule, with the exception of describes the human MHC Class II molecule of HLA-DR-BR 0401, without further description from the instant specification.

Claims 100-106, 112-117, 127 and 137 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 100-106, 112-117, 127 and 137 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide that consists of a sequence selected from the group consisting of SEQ ID NO:1, 3-4, 6, 8-12 and 18-19, a composition thereof, and a method comprising administering said peptide, does not reasonably provide enablement for the instant claims that encompass any MHC class II immunogenic peptide, or any derivative thereof, wherein said peptide consists essentially of amino acids 56-70 of SEQ ID NO:39 or amino acids 448-462 of SEQ ID NO:39 or a derivative thereof that is at least 85% identical with the immunogenic peptide, wherein the immunogenic peptide or derivative thereof is recognized by a CD4+ T lymphocyte which is restricted by a MHC Class II molecule, and a method of administering a composition comprising said peptide or derivative, wherein said peptide consists essentially of a sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:6 (claims 100, 112-117, 127 and 137), SEQ ID NO:4 (claim 101), SEQ ID NO:3 (claim 102), SEQ ID NO:10 (claim 103), SEQ ID NO:11 (claim 104), SEQ ID NO:12 (claim 105), and SEQ ID NOs: 8, 9, 18 and 19 (claim 106).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims encompass an immunogenic peptide consisting essentially of amino acids 56-70 of SEQ ID NO:39 or amino acids 448-462 of SEQ ID NO:39 or a derivative thereof that is at least 85% identical with the immunogenic peptide, wherein the immunogenic peptide or derivative thereof is recognized by a CD4+ T lymphocyte which is restricted by a MHC Class II molecule, and a method of administering a composition comprising said peptide or derivative, wherein said peptide consists essentially of a sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:6 (claims 100, 112-117, 127 and 137), SEQ ID NO:4 (claim 101), SEQ ID NO:3 (claim 102), SEQ ID NO:10 (claim 103), SEQ ID NO:11 (claim 104), SEQ ID NO:12 (claim 105), and SEQ ID NOs: 8, 9, 18 and 19 (claim 106).

The instant specification discloses peptides consisting of consisting of SEQ ID NO:1, 3-4, 6, 8-12 and 18-19, compositions thereof, and methods comprising administering said peptides. However, other than said peptides the instant specification does not provide adequate guidance and direction regarding how to make and use any immunogenic peptide consisting essentially of of amino acids 56-70 of SEQ ID NO:39 or amino acids 448-462 of SEQ ID NO:39 or a derivative thereof that is at least 85% identical with the immunogenic peptide, wherein the immunogenic peptide or derivative thereof is recognized by a CD4+ T lymphocyte which is restricted by a MHC Class II molecule, and a method of administering a composition comprising said peptide or derivative, for two reasons.

First, since the phrase "consisting essentially of" is being interpreted as comprises, as discussed supra, the recited peptide and derivative thereof, can also encompass an indeterminate number and type of additional amino acids, in addition to the amino acids set forth in the recited SEQ ID NO:s 1 and 6. It is noted that Rammensee et al (Immunogenetics (1995) 41:175-177) teaches that peptides recognized by class II restricted cells are between 12 and 25 amino acids (page 181). Due to the comprising terminology, the instant claims encompass peptides larger than just the 14-15mer peptide of SEQ ID NO:1, 3-4, 6, 8-12 and 18-19, and can encompass peptides with an indeterminate number and type of additional amino acids, which exceed the upper limit of about 25 amino acids for Class II binding by peptides taught by Rammennsee.

Second, the recitation of peptide derivatives wherein the derivative is at least 85% identical with the immunogenic peptide encompasses peptides with an indeterminate number and type of additional amino acids, and can conceivably lack the anchor residues necessary to bind MHC Class II molecules. Rammensee teaches that MHC Class II motifs generally contain 3 anchor residues, see entire article, including pages 181-182. A derivative with 85% identity with SEQ ID NO:1 or SEQ ID NO:6 allows three residues to be changed, including all htree anchor residues, which may result in a loss in the ability to bind MHC Class II.

Therefore, in view of the scope of the claims, it would require undue experimentation by one of skill in the art to predict the sequence of the additional and/or substituted amino acid residues encompassed by the claimed MHC class II restricted peptides, that retain the functional limitations of the claims, without further guidance and direction form the instant specification.

Claims 127 and 137 encompass a method of inducing CD4+ T lymphocytes in a host to respond to melanoma comprising administering a composition comprising a peptide encompassed by claim 1. The instant specification provides invitro data demonstrating the ability of the recited peptides to stimulate in vitro TILs from patients. However, the instant specification discloses no examples of administration to a mammal of any disclosed or recited peptide. Razzaque (Vaccine 19:644-647 (2001)) teaches on page 644 that tumor vaccines are therapeutic, unlike conventional vaccines for infectious diseases which are mostly preventative in nature. Therefore, it would require undue experimentation for one of skill to practice a method of preventing melanoma without additional guidance and direction from the instant specification. Furthermore, Rosenberg (Immunology Today 18(4):175-182 (1997)) teach that although tyrosinase (from which the recited peptides are derived) appears to be an antigen recognized on a variety of MHC molecules, only TILs restricted by HLA-A24 have been shown to mediate tumor regression in vivo(see entire article, especially page 178). Since Hla-A24 is a class I molecule, it would require undue experimentation for one of skill to use a pharmaceutical composition comprising any of the recited Class II peptides in a method of treating melanoma without further guidance and direction from the instant specification.

Claim Rejections - 35 USC § 102

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 100 and 116 are rejected under 35 U.S.C. 102(e) as being anticipated by Kwon, US Patent 5,679,511, Issued 10-21-1997, filed 6-1-1992.

'511 teaches a sequence (SEQ ID NO:10) that comprises SEQ IDNO:1 of the instant application (ie amino acids 56-70 of instant SEQ ID NO:39). Claim 116 is included because '511 teaches that said peptide is suspended in PBS, a pharmaceutical composition. Claim 100 and 116 are included in this rejection because of the open interpretation of the recited phrase "consisting essentially of", as discussed supra. Therefore the referenced teachings anticipate the claimed invention.

Allowable Subject Matter

Claims 107-111 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, PhD
Patent Examiner, Group 1640,
April 4, 2003

Patrick J. Nolan, PhD
Primary Patent Examiner, Group 1640,

Applicati n No.: 08/533,895

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Figures 6, 7 and 9 discloses sequences which lack SEQ ID NO: tags.

Applicant Must Provide: **ONLY** IF THE CRF/PAPR COPY SEQUENCE LISTING DOES NOT CONTAIN SAID SEQUENCEs.

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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